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1: [NP_066961](#). Reports TNF receptor-asso...[gi:22027612] BLink, Conserved Domains, Links

LOCUS NP_066961 501 aa linear PRI 27-NOV-2005
DEFINITION TNF receptor-associated factor 2 [Homo sapiens].
ACCESSION NP_066961 NP_663770
VERSION NP_066961.2 GI:22027612
DBSOURCE REFSEQ: accession NM_021138.3
KEYWORDS
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (residues 1 to 501)
AUTHORS Yang,C.H., Murti,A. and Pfeffer,L.M.
TITLE Interferon induces NF-kappa B-inducing kinase/tumor necrosis factor receptor-associated factor-dependent NF-kappa B activation to promote cell survival
JOURNAL J. Biol. Chem. 280 (36), 31530-31536 (2005)
PUBMED 16009713
REMARK GenerIF: Results for the first time place tumor necrosis factor receptor-associated factor-2 (TRAF2), previously shown to function in TNF signaling, within the interferon signal transduction pathway 2 (residues 1 to 501)
AUTHORS Esparza,E.M. and Arch,R.H.
TITLE Glucocorticoid-induced TNF receptor, a costimulatory receptor on naive and activated T cells, uses TNF receptor-associated factor 2 in a novel fashion as an inhibitor of NF-kappa B activation
JOURNAL J. Immunol. 174 (12), 7875-7882 (2005)
PUBMED 15944293
REMARK GenerIF: In contrast with its effects on signaling triggered by other TNF receptors, functional studies reveal that TRAF2 plays a novel inhibitory role in glucocorticoid-induced TNF receptor (GITR)-triggered NF-kappa B activation.
REFERENCE 3 (residues 1 to 501)
AUTHORS Kim,W.J., Back,S.H., Kim,V., Ryu,I. and Jang,S.K.
TITLE Sequestration of TRAF2 into stress granules interrupts tumor necrosis factor signaling under stress conditions
JOURNAL Mol. Cell. Biol. 25 (6), 2450-2462 (2005)
PUBMED 15743837
REMARK GenerIF: TRAF2 colocalizes with eIF4GI in insoluble stress granules during cellular exposure to stress conditions.
REFERENCE 4 (residues 1 to 501)
AUTHORS Hauer,J., Puschner,S., Ramakrishnan,P., Simon,U., Bongers,M., Federle,C. and Engelmann,H.
TITLE TNF receptor (TNFR)-associated factor (TRAF) 3 serves as an inhibitor of TRAF2/5-mediated activation of the noncanonical NF-kappaB pathway by TRAF-binding TNFRs
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 102 (8), 2874-2879 (2005)
PUBMED 15708970
REMARK GenerIF: TRAF3 specifically blocked the NF-kappaB activation via TRAF2/5.
REFERENCE 5 (residues 1 to 501)
AUTHORS He,L., Grammer,A.C., Wu,X. and Lipsky,P.E.
TITLE TRAF3 forms heterotrimers with TRAF2 and modulates its ability to mediate NF- $\{\kappa\}$ B activation
JOURNAL J. Biol. Chem. 279 (53), 55855-55865 (2004)
PUBMED 15383523
REMARK GenerIF: there is a novel association between TRAF2 and TRAF3 that is mediated by unique portions of each protein and that specifically regulates activation of NF-kappaB, but not AP-1
REFERENCE 6 (residues 1 to 501)
AUTHORS Zhang,H., Zhang,R., Luo,Y., D'Alessio,A., Pober,J.S. and Min,W.
TITLE AIP1/DAB2IP, a novel member of the Ras-GAP family, transduces TRAF2-induced ASK1-JNK activation
JOURNAL J. Biol. Chem. 279 (43), 44955-44965 (2004)
PUBMED 15310755
REMARK GenerIF: AIP1 is a novel transducer in TNF-induced TRAF2-dependent activation of ASK1 that mediates a balance between JNK versus

REFERENCE
 AUTHORS Vischioni,B., Giaccone,G., Span,S.W., Kruty,F.A. and Rodriguez,J.A.
 TITLE Nuclear shuttling and TRAF2-mediated retention in the cytoplasm
 regulate the subcellular localization of cIAP1 and cIAP2
 JOURNAL Exp. Cell Res. 298 (2), 535-548 (2004)
 PUBMED 15265700
 REMARK GeneRIF: TRAF2 plays an important role as regulator of IAP
 nucleocytoplasmic localization, by preventing nuclear translocation
 of cIAP1 and cIAP2.

REFERENCE
 AUTHORS Fotin-Mleczek,M., Henkler,F., Haussler,A., Glauner,H., Samel,D.,
 Graness,A., Scheurich,P., Mauri,D. and Wajant,H.
 TITLE Tumor necrosis factor receptor-associated factor (TRAF) 1 regulates
 CD40-induced TRAF2-mediated NF-kappaB activation
 JOURNAL J. Biol. Chem. 279 (1), 677-685 (2004)
 PUBMED 14557256
 REMARK GeneRIF: stoichiometry of TRAF1-TRAF2 heteromeric complexes
 ((TRAF2)2-TRAF1 versus TRAF2-(TRAF1)2) determines their capability
 to mediate CD40 signaling but has no major effect on TNF signaling
 9 (residues 1 to 501)
 JOURNAL Sakurai,H., Suzuki,S., Kawasaki,N., Nakano,H., Okazaki,T.,
 Chino,A., Doi,T. and Saiki,I.
 PUBMED 12842894
 REMARK GeneRIF: TRAF2 has a role in TNF-alpha induced IKK phosphorylation
 of NF-kappaB p65

REFERENCE
 AUTHORS Kaneko,M., Niinuma,Y. and Nomura,Y.
 TITLE Activation signal of nuclear factor-kappa B in response to
 endoplasmic reticulum stress is transduced via IRE1 and tumor
 necrosis factor receptor-associated factor 2
 JOURNAL Biol. Pharm. Bull. 26 (7), 931-935 (2003)
 PUBMED 12843613
 REMARK 11 (residues 1 to 501)
 Shi,C.S. and Kehrl,J.H.
 TITLE Tumor necrosis factor (TNF)-induced germinal center kinase-related
 (GCKR) and stress-activated protein kinase (SAPK) activation
 depends upon the E2/E3 complex Ubc13-Uev1A/TNF receptor-associated
 factor 2 (TRAF2)
 JOURNAL J. Biol. Chem. 278 (17), 15429-15434 (2003)
 PUBMED 12591926
 REMARK GeneRIF: TNF signaling leads to oligomerization, ubiquitination,
 and activation of GCKR and activation of the SAPK pathway in a
 manner that depends upon TRAF2 polyubiquitination and
 oligomerization and Ubc13 function

REFERENCE
 AUTHORS Kuai,J., Nickbarg,E., Wooters,J., Qiu,Y., Wang,J. and Lin,L.L.
 TITLE Endogenous association of TRAF2, TRAF3, cIAP1, and Smac with
 lymphotoxin beta receptor reveals a novel mechanism of apoptosis
 JOURNAL J. Biol. Chem. 278 (16), 14363-14369 (2003)
 PUBMED 12571250
 REMARK GeneRIF: TRAF2, TRAF3, cIAP1, Smac, and lymphotoxin beta receptor
 associate and are involved in apoptosis

REFERENCE
 AUTHORS Munzert,G., Kirchner,D., Stobbe,H., Bergmann,L., Schmid,R.M.,
 Dohner,H. and Heimpel,H.
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 JOURNAL Blood 100 (10), 3749-3756 (2002)
 PUBMED 12411322
 REMARK 14 (residues 1 to 501)
 Habelhah,H., Frew,I.J., Laine,A., Janes,P.W., Relaix,F.,
 Sassoone,D., Bowtell,D.D. and Ronai,Z.
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 JOURNAL EMBO J. 21 (21), 5756-5765 (2002)
 PUBMED 12411493
 REMARK 15 (residues 1 to 501)
 Zhou,R., Bonneaud,N., Yuan,C.X., de Santa Barbara,P., Boizet,B.,
 Schomber,T., Scherer,G., Roeder,R.G., Poulat,F. and Berta,P.
 TITLE SOX9 interacts with a component of the human thyroid hormone
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 JOURNAL Nucleic Acids Res. 30 (14), 3245-3252 (2002)
 PUBMED 12136106
 REMARK 16 (residues 1 to 501)
 Brown,K.D., Hostager,B.S. and Bishop,G.A.
 TITLE Regulation of TRAF2 signaling by self-induced degradation
 JOURNAL J. Biol. Chem. 277 (22), 19433-19438 (2002)
 PUBMED 11909853

REFERENCE 17 (sites)
 AUTHORS Brown,K.D., Hostager,B.S. and Bishop,G.A.
 TITLE Regulation of TRAF2 signaling by self-induced degradation
 JOURNAL J Biol Chem 277 (22), 19433-19438 (2002)
 PUBMED 11909853

REFERENCE 18 (residues 1 to 501)
 AUTHORS Eliopoulos,A.G., Davies,C., Blake,S.S., Murray,P., Najafipour,S., Tsichlis,P.N. and Young,L.S.
 TITLE The oncogenic protein kinase Tpl-2/Cot contributes to Epstein-Barr virus-encoded latent infection membrane protein 1-induced NF-kappaB signaling downstream of TRAF2
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 PUBMED 11932422

REFERENCE 19 (residues 1 to 501)
 AUTHORS Hostager,B.S. and Bishop,G.A.
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 JOURNAL J. Immunol. 168 (7), 3318-3322 (2002)
 PUBMED 11907088

REFERENCE 20 (residues 1 to 501)
 AUTHORS Li,X., Yang,Y. and Ashwell,J.D.
 TITLE TNF-RII and c-IAP1 mediate ubiquitination and degradation of TRAF2
 JOURNAL Nature 416 (6878), 345-347 (2002)
 PUBMED 11907583

REMARK GenERIF: TNF-RII and c-IAP1 mediate its ubiquitination

REFERENCE 21 (sites)
 AUTHORS Li,X., Yang,Y. and Ashwell,J.D.
 TITLE TNF-RII and c-IAP1 mediate ubiquitination and degradation of TRAF2
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REFERENCE 22 (residues 1 to 501)
 AUTHORS Cao,H., Courchesne,W.E. and Mastick,C.C.
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 JOURNAL J. Biol. Chem. 277 (11), 8771-8774 (2002)
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 AUTHORS Xia,P., Wang,L., Moretti,P.A., Albanese,N., Chai,F., Pitson,S.M., D'Andrea,R.J., Gamble,J.R. and Vadas,M.A.
 TITLE Sphingosine kinase interacts with TRAF2 and dissects tumor necrosis factor-alpha signaling
 JOURNAL J. Biol. Chem. 277 (10), 7996-8003 (2002)
 PUBMED 11777919

REMARK GenERIF: These findings show a role for SphK in the signal transduction by TRAF2 specifically leading to activation of NF-kappa B and antiapoptosis.

REFERENCE 24 (residues 1 to 501)
 AUTHORS Yan,M., Zhang,Z., Brady,J.R., Schilbach,S., Fairbrother,W.J. and Dixit,V.M.
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 JOURNAL Curr. Biol. 12 (5), 409-413 (2002)
 PUBMED 11882293

REFERENCE 25 (residues 1 to 501)
 AUTHORS Kanamori,M., Suzuki,H., Saito,R., Muramatsu,M. and Hayashizaki,Y.
 TITLE T2BP, a novel TRAF2 binding protein, can activate NF-kappaB and AP-1 without TNF stimulation
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 PUBMED 11798190

REFERENCE 26 (residues 1 to 501)
 AUTHORS Oukka,M., Kim,S.T., Lugo,G., Sun,J., Wu,L.C. and Glimcher,L.H.
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 PUBMED 11804591

REFERENCE 27 (residues 1 to 501)
 AUTHORS Wiley,S.R., Cassiano,L., Lofton,T., Davis-Smith,T., Winkles,J.A., Lindner,V., Liu,H., Daniel,T.O., Smith,C.A. and Fanslow,W.C.
 TITLE A novel TNF receptor family member binds TWEAK and is implicated in angiogenesis
 JOURNAL Immunity 15 (5), 837-846 (2001)
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REFERENCE 28 (residues 1 to 501)
 AUTHORS Choi,Y.H., Kim,K.B., Kim,H.H., Hong,G.S., Kwon,Y.K., Chung,C.W., Park,Y.M., Shen,Z.J., Kim,B.J., Lee,S.Y. and Jung,Y.K.
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REFERENCE 29 (residues 1 to 501)
 AUTHORS Lieberson,R., Mowen,K.A., McBride,K.D., Leautaud,V., Zhang,X., Suh,W.K., Wu,L. and Glimcher,L.H.
 TITLE Tumor necrosis factor receptor-associated factor (TRAF)2 represses

the T helper cell type 2 response through interaction with NFAT-interacting protein (NIP45)
 J. Exp. Med. 194 (1), 89-98 (2001)
11435475

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TITLE A diverse family of proteins containing tumor necrosis factor receptor-associated factor domains
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TITLE IL-15/IL-15Ralpha intracellular trafficking in human melanoma cells and signal transduction through the IL-15Ralpha
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JOURNAL	Rietschoten, J.G., Dewulf, N., de Boer, M., Vandenabeele, P., Huylebroeck, D. and Remacle, J.E.
PUBMED	10764746
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AUTHORS	Eby, M.T., Jasmin, A., Kumar, A., Sharma, K. and Chaudhary, P.M.
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REFERENCE	42 (residues 1 to 501)
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AUTHORS	Leonardi, A., Ellinger-Ziegelbauer, H., Franzoso, G., Brown, K. and Siebenlist, U.
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JOURNAL	J. Biol. Chem. 275 (1), 271-278 (2000)
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REFERENCE	45 (residues 1 to 501)
AUTHORS	Pomerantz, J.L. and Baltimore, D.
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JOURNAL	EMBO J. 18 (23), 6694-6704 (1999)
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REFERENCE	46 (residues 1 to 501)
AUTHORS	Fu, C.A., Shen, M., Huang, B.C., Lasaga, J., Payan, D.G. and Luo, Y.
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AUTHORS	Ye, X., Mehlen, P., Rabizadeh, S., VanArsdale, T., Zhang, H., Shin, H., Wang, J.J., Leo, E., Zapata, J., Hauser, C.A., Reed, J.C. and Bredesen, D.E.
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AUTHORS	Hoeflich, K.P., Yeh, W.C., Yao, Z., Mak, T.W. and Woodgett, J.R.
TITLE	Mediation of TNF receptor-associated factor effector functions by apoptosis signal-regulating kinase-1 (ASK1)
JOURNAL	Oncogene 18 (42), 5814-5820 (1999)
PUBMED	10523862
REFERENCE	49 (residues 1 to 501)
AUTHORS	Chin, A.I., Shu, J., Shan Shi, C., Yao, Z., Kehrl, J.H. and Cheng, G.
TITLE	TANK potentiates tumor necrosis factor receptor-associated factor-mediated c-Jun N-terminal kinase/stress-activated protein kinase activation through the germinal center kinase pathway
JOURNAL	Mol. Cell. Biol. 19 (10), 6665-6672 (1999)
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AUTHORS	Shi, C.S., Leonardi, A., Kyriakis, J., Siebenlist, U. and Kehrl, J.H.
TITLE	TNF-mediated activation of the stress-activated protein kinase pathway: TNF receptor-associated factor 2 recruits and activates germinal center kinase related
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PUBMED	10477597
REFERENCE	51 (residues 1 to 501)
AUTHORS	McWhirter, S.M., Pullen, S.S., Holton, J.M., Crute, J.J., Kehry, M.R. and Alber, T.
TITLE	Crystallographic analysis of CD40 recognition and signaling by human TRAF2
JOURNAL	Proc. Natl. Acad. Sci. U.S.A. 96 (15), 8408-8413 (1999)

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 AUTHORS Yu, P.W., Huang, B.C., Shen, M., Quast, J., Chan, E., Xu, X., Nolan, G.P., Payan, D.G. and Luo, Y.
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 PUBMED 10339433
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 AUTHORS Baud, V., Liu, Z.G., Bennett, B., Suzuki, N., Xia, Y. and Karin, M.
 TITLE Signaling by proinflammatory cytokines: oligomerization of TRAF2 and TRAF6 is sufficient for JNK and IKK activation and target gene induction via an amino-terminal effector domain
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 AUTHORS Kwon, B., Yu, K.Y., Ni, J., Yu, G.L., Jang, I.K., Kim, Y.J., Xing, L., Liu, D., Wang, S.X. and Kwon, B.S.
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 AUTHORS Kim, H.H., Lee, D.E., Shin, J.N., Lee, Y.S., Jeon, Y.M., Chung, C.H., Ni, J., Kwon, B.S. and Lee, Z.H.
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 AUTHORS MacLachlan, T.K., Sang, N., De Luca, A., Puri, P.L., Levrero, M. and Giordano, A.
 TITLE Binding of CDK9 to TRAF2
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 AUTHORS Wong, B.R., Josien, R., Lee, S.Y., Vologodskaia, M., Steinman, R.M. and Choi, Y.
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 TITLE NF-κB antiapoptosis: induction of TRAF1 and TRAF2 and c-IAP1 and c-IAP2 to suppress caspase-8 activation
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 REFERENCE 60 (residues 1 to 501)
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 TITLE ASK1 is essential for JNK/SAPK activation by TRAF2
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 AUTHORS Yuasa, T., Ohno, S., Kehrl, J.H. and Kyriakis, J.M.
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 AUTHORS Thome, M., Hofmann, K., Burns, K., Martinon, F., Bodmer, J.L., Mattmann, C. and Tschopp, J.
 TITLE Identification of CARDIAK, a RIP-like kinase that associates with caspase-1
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 cytoplasmic domain of the 75 kDa tumor necrosis factor receptor
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 On or before Feb 13, 2004 this sequence version replaced
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Summary: The protein encoded by this gene is a member of the TNF
 receptor associated factor (TRAF) protein family. TRAF proteins
 associate with, and mediate the signal transduction from members of
 the TNF receptor superfamily. This protein directly interacts with
 TNF receptors, and forms a heterodimeric complex with TRAF1. This
 protein is required for TNF-alpha-mediated activation of MAPK8/JNK
 and NF-kappaB. The protein complex formed by this protein and TRAF1
 interacts with the inhibitor-of-apoptosis proteins (IAPs), and
 functions as a mediator of the anti-apoptotic signals from TNF
 receptors. The interaction of this protein with TRADD, a TNF
 receptor associated apoptotic signal transducer, ensures the
 recruitment of IAPs for the direct inhibition of caspase
 activation. BIRC2/c-IAP1, an apoptosis inhibitor possessing
 ubiquitin ligase activity, can ubiquitinate and induce the
 degradation of this protein, and thus potentiate TNF-induced
 apoptosis. Multiple alternatively spliced transcript variants have
 been found for this gene, but the biological validity of only one
 transcript has been determined.

Location/Qualifiers

FEATURES

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